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Commissioner for Patents
United States Patent and Trademark Office
Washington, DC 20231

24 September 2001

Dear Commissioner,

Along with this letter I am submitting four articles as additional material in support of our patent request. App. No.: 09/691,671, filing date: 10/18/2000, Name of Applicant: Michael J. Wilcox, Title of Invention: "C-shaped cross section tubular ophthalmic implant for reduction of intraocular pressure in glaucomatous eyes and method of use."

This material may not be readily available outside the ophthalmic community, in the glaucoma specialty. The first two peer-reviewed articles, authored by the applicant, appeared in 2001. The *Journal of Mathematical Modeling and Scientific Computing 13*: 22-27 presents a model for a fiber-reinforced composite material with the ideal orientation of reinforcing structure and evidence that the tissue collagen composite lays down precisely this configuration. The second, from the Proceedings of the Rocky Mountain Bioengineering Symposium, 2001, appeared in *Biomedical Sciences Instrumentation 37*: 257-62 and introduces a positive feedback model that we tested and presented evidence for. This model explains why the large plate devices fail and why our new design has better performance and should not fail, due to our use of geometry to reduce surface tension.

The third publication appeared in *Glaucoma 2000: Cutting–Edge Diagnosis and Therapy* from the American Academy of Ophthalmology and the American Glaucoma Society and presents the current thinking about shunt implants in treatment of glaucoma and quotes our Journal of Glaucoma 2000 paper. The author is Ann Louise Coleman, MD, PhD. She has grasped the implication of our 2000 paper but does not accept the described principle or that this approach is a direct implementation of Laplace's Law. Her response is typical of the ophthalmic community, which still views our findings as an interesting untested theory. Our new study should help to solidify our position. We now present the first evidence that surface tension is proportional to capsule thickness and, therefore, hydraulic conductivity. Likewise, the Food and Drug Administration will not accept our argument that the filtration mechanism is the same for cylinders and large-plate shunt devices. The fact that I am first author on both papers that demonstrated the filtration mechanism for Molteno implants in primate eyes and cylindrical implants in rabbit eyes, using the same experimental protocols, does not matter. They do not accept that we have only changed the geometry in order to get improved performance. Their position in writing is that if it looks different from accepted shunt implants, it is different and cannot be approved for marketing until it has passed clinical testing and been shown to perform at least as well as the state of the art. Therefore, the community does not even accept the hypothesis we proposed in our 1994 Journal of Glaucoma paper. In 1994, we believed and stated that capsule thickness appeared to be a function of the healing process in primate eyes but that reduced surface tension would prevent capsule fibrosis, leading to longer lifetimes for the implant. Therefore, the only apparent advantage of the new design at that time was decrease volume of the device and subsequent complication avoidance with extraocular muscles. Only after we had tested the device in animals did we discover that capsule thickness was proportional

to surface tension. Only now that we have examined this relationship in other large-plate shunt implants using the same animal model can we show a quantitative relationship.

The fourth article is a preprint of a journal article we have sent out for initial review and intend to submit to the *Journal of Glaucoma*. We are also requesting Food and Drug Administration approval for an Investigational Device Exemption so that we can begin clinical trials of the device. We have found a manufacturer for the device and intend to request grant support for a limited clinical trial in the United States, involving 5 academic medical centers, and a larger study planned in Southern China, involving 500 patients.

Along with the patent application we submitted a *Journal of Glaucoma* article that appeared in Volume 9, number 1, February 2000, pages 74-82, entitled, "Performance of a new, low-volume, high-surface area aqueous shunt in normal rabbit eyes." The authors were MJ Wilcox et al. That article described the first use of the implant in animal eyes, showed histological evidence for improved performance and constituted the proof-of-concept in animal studies. In the new study we report a comparative analysis using ultrastructural examination of capsules formed around the major shunt implants (including Molteno, Baerveldt, and Ahmed implants) and our new, cylindrical implants in animal eyes. This study shows the differences underlying the structure and function of these capsules and explains why the new technology is superior to the old technology. We think these new results will allow the patent examiner to better determine the differences in approach with accepted shunt devices and to understand the differences the new technology will provide to treatment of glaucoma in humans. The new results provide a quantitative assessment of filtration in large plate devices and compare them with the new technology. We provide a structural and functional reasons underlying improved performance. This supplemental information will bolster our claims and support our reduction to practice.

All large plate shunt devices experience significant problems. The 2 most frequently occurring complications are initial postoperative hypotony and early failure of the device as a filtration membrane due to capsular fibrosis. The analysis provides a framework for assessment of filtration efficiency in other implants and demonstrates the reason for their failure, consistent with results from clinical studies. It also describes the underlying structure and function of the new device and shows how the new device will overcome the initial hypotony and overcome the fibrosis that causes failure inherent with the other shunt devices.

Sincerely,

Michael Wilcox, PhD
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